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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,661	09/23/2003	Jean-Claude Yvin	P08424US00/BAS	1057

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1623	

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10/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,661	YVIN ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/23/08 has been entered.

The following office action is a responsive to the amendment filed, 07/23/08.

The amendment filed 07/23/08 affects the application, 10/668,661 as follows:

1. Claim 23 has been amended. The rejection of the prior office action mailed 03/17/08 is maintained.
2. The responsive to applicants' arguments is contained herein below.

Claims 23-34 are pending in the application

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuzuki et al. (Bioscience, Biotechnology, and Biochemistry, (1999 Jan) Vol. 63, No. 1, pages 104-110) in view of Fan et al. (Zhongguo Yaoke Daxue Xuebao (1988), 19 (1), pages 30-34) (Abstract Only).

In claim 23, applicant claims a method of promoting the regeneration of the cells in the bone marrow and the peripheral blood of a patient said patient being subjected to a chemotherapeutic antineoplastic treatment comprising administration to said patient of an effective amount of an antineoplastic agent that causes an acute reduction of said cells, said method comprising administration of laminarin to the patient in an amount effective to cause promotion of the regeneration of the cells, the laminarin being administered in conjunction with the administration of the antineoplastic agent, wherein said laminarin has a molecular weight from about 2,500 to about 6,000. Claim 24 is drawn the method of claim 23, wherein the antineoplastic agent is cyclophosphamide. Claims 25 and 26 are drawn to said method wherein laminarin is administered by specific routes. Claims 27 and 28 are drawn to said method wherein laminarin is administered before, simulataneously with or after the antineoplastic agent or the cyclophosphamide. Claims 17-22 are drawn to said method wherein laminarin is soluble laminarin.

Tsuzuki et al. disclose a method of promoting the formation (regeneration) of blood marrow cells (hematopoiesis) of a patient (mice), said patient being subjected to a chemotherapeutic antineoplastic treatment comprising administration to said patient of an effective amount of an antineoplastic agent (cyclophosphamide) which causes an acute reduction of the said cells (leukopenia) due to the effect of the antineoplastic agent (cyclophosphamide), said method comprising administering a soluble glucan to the patient in an amount effective to cause the promotion of the formation (regeneration) of blood cells, said glucan being administered in conjunction with the administration of the antineoplastic agent (cyclophosphamide) (see abstract). Furthermore, Tsuzuki et al. disclose that the said glucan

increase hematopoietic responses or exhibits hematopoietic activity (i.e. they promote the formation (regeneration) of blood cells) (see abstract). In addition, Tsuzuki et al. suggest that the conformation of the glucans are independent of the hematopoietic response caused by the glucans (see abstract).

The difference between applicant's claimed method and Tsuzuki et al.'s method is that Tsuzuki et al. do not use the specific glucan, laminarin.

Fan et al. disclose that the glucan, laminarin, exhibits remarkable antagonistic action to leukopenia and remarkable antiradiation effect (see abstract). This implies that the glucan, laminarin oppose, prevent or act against an acute reduction of the said cells (leukopenia).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Tsuzuki et al. and Fan et al., to have used the method of Tsuzuki et al. to promote the regeneration of the cells in the bone marrow and the peripheral blood of a patient who is being subjected to a chemotherapeutic antineoplastic treatment of a antineoplastic agent such as cyclophosphamide that causes the said reduction, by administering the glucan, laminarin of different molecular weights since Tsuzuki et al. disclose that glucans (which includes laminarin) promote the formation (regeneration) of blood cells and Fan et al. teach that the glucan, laminarin, also opposes, prevent or act against an acute reduction of the said cells (leukopenia).

One having ordinary skill in the art would have been motivated in view of Tsuzuki et al. and Fan et al., to have used the method of Tsuzuki et al. to promote the regeneration of the cells in the bone marrow and the peripheral blood of a patient who is being subjected to a chemotherapeutic antineoplastic treatment of a antineoplastic agent such as cyclophosphamide

that causes the said reduction, by administering the glucan, laminarin of different molecular weights, based on factors such as the type, and/or severity of the leukopenia caused by said treatment, and since Tsuzuki et al. disclose that glucans (which includes laminarin) promote the formation (regeneration) of blood cells and Fan et al. teach that the glucan, laminarin, also opposes, prevent or act against an acute reduction of the said cells (leukopenia). It should be noted that the use of specific routes and ways of administration of said composition is common and obvious in the art, and is well within the purview of a skilled artisan.

Response to Arguments

Applicant's arguments with respect to claim 23-34 have been considered but are not found convincing.

The applicant argues that even if these results may suggest a potent activity of SPG and SPG-OH on hematopoieisis, further in vivo results would have been necessary to convince one skilled in the art that SPG and SPG-OH could stimulate the regeneration of cells in the bone marrow and the peripheral blood. On the contrary however, Tsuzuki et al. disclose that the said glucan increase hematopoietic responses or exhibits hematopoietic activity (i.e. they promote the formation (regeneration) of blood cells) (see above rejection). Consequently, further in vivo results would not have been necessary to convince one skilled in the art that SPG and SPG-OH could stimulate the regeneration of cells in the bone marrow and the peripheral blood.

The applicant argues that the results obtained with Sonifilan cannot be obviously extrapolated to Laminarin, and vice versa. However, the rejection was made by combining Tsuzuki et al. and Fan et al. references. Furthermore, Tsuzuki et al. suggest that the conformation of the glucans are independent of the hematopoietic response caused by the

glucans (see abstract). Consequently, a skilled artisan reasonable expect that glucans of different conformation would also produce an increase hematopoietic responses or exhibits hematopoietic activity (i.e. promote the formation (regeneration) of blood cells) as set forth above.

The applicant argues that the laminarin of the claimed invention is dramatically different from Fan et al.'s laminarin (e.g., in terms of molecular weight). However, the use of laminarin of different molecular weights, depends on factors such as the type, and/or severity of the leukopenia caused by said treatment.

The applicant argues that the laminarin of the claimed invention is preferably extracted from *Laminaria digitata* or *Laminaria saccharina* (see page 6, lines 13-30), whereas the polysaccharide of Fan et al. is extracted from *Luminaria japonica.* However, the compound of the claimed invention and the compound of Fan et al. are both laminarin regardless of the source from which they are obtained. Furthermore, the use of laminarin of different molecular weights, depends on factors such as the type, and/or severity of the leukopenia caused by said treatment.

The applicant argues that the laminarin of the claimed invention is only composed of glucopyranose units (see e.g., page 4, lines 25-29) and the terminal unit of the main chain consists of glucose or mannitol (see e.g., page 5, lines 1-3). To the contrary, the "laminarin" of Fan et al. only contains 60.4% of sugars, the remaining 39.6% being undefined, but may be, as far as the Fan et al. reference is understandable, proteins and nucleic acids. However, applicant's method claims do not require the use of laminarin of any specific composition such as specific sugar or glucopyranose units. It should also be noted that Fan et al.'s reference that the laminarin or polysaccharides is without protein and nucleic acid (see abstract).

The applicant argues that the laminarin of the claimed invention is safe and presents an acute toxicity LD50 in the rat greater than 2,000mg/kg (see e.g., page 15, lines 3-5). Conversely, the "laminarin" of Fan et al. presents an acute toxicity LD50 in mice of 980mg/kg, which constitutes a huge difference of more than two fold. However, the said acute toxicity LD50 for applicant's claimed laminarin and that of Fan et al. were not determined under the same conditions. For example, applicant's laminarin were administered orally whereas Fan et al.'s laminarin were injected. Furthermore, the use of laminarin of different molecular weights, depends on factors such as the type, and/or severity of the leukopenia caused by said treatment.

The applicant argues that even if the polysaccharide of Fan et al. may have an antagonistic action on leucopenia, one having ordinary skill in this art would not have concluded anything concerning the activity of the laminarin of the claimed invention. However, Fan et al. disclose that the glucan, laminarin, exhibits remarkable antagonistic action to leukopenia and remarkable antiradiation effect (see above rejection). This implies that the glucan, laminarin oppose, prevent or act against an acute reduction of the said cells (leukopenia). Thus, one of ordinary skill in the art would be motivated even further to use the glucan laminarin so as to facilitate the said promotion of the formation (regeneration) of blood cells.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be

reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
October 9, 2008.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner
Art Unit 1623